REMARKS

I. Status of the Claims

Claims 1-20 were originally filed. Claims 21-29 were later added. Claims 1-29 are currently pending and stand rejected.

II. Claim Rejection

In the final Office Action (mailed April 9, 2003) and the Advisory Action (mailed November 17, 2003), the Examiner maintained the rejection of claims 1-29 under 35 U.S.C. §103(a) for alleged obviousness over Margolskee *et al.*, Bruch *et al.*, Levine *et al.* or Ray *et al.*, and Negulescu *et al.* Applicants respectfully traverse the rejection.

To establish a *prima facie* case of obviousness, three basic criteria must be met: first, the prior art references must teach or suggest all the claim limitations; second, there must be some suggestion or motivation, either in the references or in the knowledge generally available to one of ordinary skill in the art, to combine the limitations; third, there must be a reasonable expectation of success in combining the limitations. MPEP §2143.

Among all pending claims, claims 1 and 20 are independent claims. Claim 1 is drawn to a method for identifying a compound that modulates taste signaling in taste cells. The method comprises two steps: (i) contacting the compound with a taste cell specific G-protein beta polypeptide, which has a greater than 70% amino acid sequence identity to SEQ ID NO:3 or SEQ ID NO:5; and (ii) determining the functional effect of the compound upon the polypeptide. Claim 20 is also drawn to a method for identifying a compound that modulates taste signaling in taste cells. The method comprises four steps: (i) expressing a taste cell specific G-protein beta polypeptide in a host cell, wherein the G-protein beta polypeptide has greater than 70% amino acid sequence identity to SEQ ID NO:3 or SEQ ID NO:5; (ii) expressing a promiscuous G-protein alpha polypeptide and a taste cell specific G-protein coupled receptor in the host cell; (iii) contacting the host cell with the compound that modulates taste signaling in taste; and (iv) determining changes in intracellular calcium levels in the host cell, thereby identifying the compound that modulates taste signaling in taste cells.

As previously stated, Margolskee discloses Gustducin, a G-protein alpha subunit specifically expressed in taste cells. Margolskee also teaches generally that taste-modulating compounds may be identified using assays for taste cell specific proteins involved in taste transduction, such as Gustducin. ***Margolskee does not disclose the taste cell specific G-protein beta subunits of the present invention, e.g., SEQ ID NO:3 or SEQ ID NO:5.***

Bruch teaches that a common G-protein beta subunit is involved in the signal transduction of taste cells. ***Bruch does not disclose the amino acid sequence of the G-protein beta subunit.***

Ray and Levine disclose two G-protein beta subunits that are 100% identical to SEQ ID NO:3 and 97% identical to SEQ ID NO:5, respectively. The polypeptide of Ray was cloned from a heart cDNA library, and expression of the mRNA encoding the G-protein beta subunit was shown in heart and brain. The polypeptide of Levine was cloned from a retina cDNA library, and expression was shown in four different cell lines: rhabdomyosarcoma, pheochromocytoma, neuroblastoma, and dermal fibroblasts. ***Neither Ray nor Levine discloses that the G-protein beta subunits are expressed in taste cells of the tongue.***

Negulescu discloses generally the use of promiscuous G-proteins for identifying G-proteins, their ligands, and compounds capable of modulating signal transduction. ***Negulscu does not specifically relate to the use of promiscuous G-protein in the method claimed in the present application.***

In considering the above cited references, the Examiner has not identified a specific motivation or suggestion in the references for one of skill in the art to combine the claim limitations. Neither has the Examiner established a reasonable expectation of success in combining the claim limitations.

In maintaining the obviousness rejection, the Examiner stated that Margolskee "does provide a suggestion that compounds that modulate either α, β, or γ [subunit] have commercial value in food and pharmaceutical" and therefore "there was motivation and also a reasonable expectation of success in the art for identifying compounds that modulate taste signal

transduction" (Advisory Action of November 17, 2004, page 3, lines 6-9). Applicants cannot agree.

Margolskee teaches a method for identifying taste modulating compounds using a G-protein, gustducin, with focus on its α subunit. This teaching at best provides a general motivation for one of skill in the art ***to try*** to establish a method for identifying taste modulating compounds using a G-protein β subunit present in taste cells. It does not provide a specific motivation for an artisan to use the G-protein β subunit of the present invention in such a screening method. Therefore, the Margolskee reference does not provide a motivation to combine the limitations of the claims.

Furthermore, it is well settled that "obvious to try" is not the proper standard for obviousness. See, *e.g.*, *N.V. Akzo v. E.I. du Pont de Nemours & Co.*, 1 USPQ2d 1704, 1707 (Fed. Cir. 1987); *in re O'Farrell*, 7 USPQ2d 1673, 1680-1681 (Fed. Cir. 1988). Because of the number and diversity of G-proteins and the complex makeup of G-proteins (each having one α, one β, and one γ subunits), there simply can be no reasonable expectation of success when one uses a different G-protein subunit in a method taught by Margolskee in an attempt to identify compounds capable of modulating taste signaling.

Applicants contend that Bruch *et al.* provides no amino acid sequence and it is therefore not known whether Bruch's G-protein is the same as the G-protein of the present invention or whether Bruch's G-protein is even related to the G-proteins described by Ray or Levine. The Examiner dismissed this argument, insisting that the amino acid sequence of the Bruch's G-protein is inherently provided, "because Bruch *et al.* clearly identify their protein as the β-protein and it is well within the knowledge of those skilled in the art to determine the amino acid sequence of a protein" (Advisory Action of November 17, 2003, page 3, first full paragraph). The Examiner's reasoning is flawed and the obviousness standard applied is incorrect.

First of all, the Examiner's reasoning appears to be based on the assumption that there is only one G-protein β subunit involved in taste signal transduction in taste cells. Although Bruch *et al.* disclose that a common G-protein β subunit is involved in the signal

transduction pathways tested in their study, this reference does not exclude the possibility that other G-protein β subunits are also involved in taste signaling. Therefore, the Examiner has not established that Bruch's G-protein β subunit is the one and the same as the G-protein β subunit of the present invention. The assertion that the amino acid sequence is an inherent property thus has no proper basis.

Secondly, even if the G-protein β subunit described by Bruch *et al.* were properly established to be the same as the β subunit of the present invention, the actual amino acid sequence of the β subunit still would not be obvious simply because of the description of the polypeptide and the well known techniques that can be used to determine the polypeptide's amino acid sequence. This is a fact pattern that can be analogized to *in re Bell*, 26 USPQ2d 1529 (Fed. Cir. 1993), and *in re Deuel*, 34 USPQ2d 1211 (Fed. Cir. 1995).

In the first case, Bell sought to claim the polynucleotide sequences encoding insulin-like growth factors (IGF) I and II, the amino acid sequences of which had been disclosed in the prior art. The PTO rejected the claims on the basis that the DNA sequence encoding a protein of a known amino acid sequence is obvious, because the method of isolating a polynucleotide encoding a known amino acid sequence is routine. The Federal Circuit reversed the rejection, holding that no *prima facie* obviousness is established because there could be a very large number of possible DNA sequences that would encode the same amino acid sequence. This is precisely the situation here: given the description of a protein's physical, chemical, and physiological properties (such as the description of a taset cell G-protein β subunit in the Bruch reference), there still can be numerous potential amino acid sequences, each different yet constituting a protein of the same characteristics. These sequences may include the variants, homologs, and mutants of any given amino acid sequence of this protein. Any particular amino acid sequence, such as SEQ ID NO:3 or SEQ ID NO:5, thus cannot be obvious according to *in re Bell*.

In the second case, Deuel sought to claim the polynucleotide sequence encoding a heparin-binding growth factor (HBGF) found in bovine uterine. The PTO rejected the claims for obviousness. The PTO reasoned that since prior art has disclosed a heparin-binding protein with

similar characteristics including the same first 19 amino acids, and the techniques for cloning a DNA coding sequence based on a partial amino acid sequence is well known, Deuel's DNA sequence is *prima facie* obvious. The Federal Circuit reversed the rejection, holding that the polynucleotide sequence cannot be conceived until one actually clones the sequence and that "[w]hat cannot be contemplated or conceived cannot be obvious." 34 USPQ2d at 1215. The same reasoning is also appropriate for the situation in the present application. The amino acid sequence of a G-protein β subunit cannot be contemplated by an artisan based on the description of such a β subunit provided by Bruch *et al.*, no matter how routine the process is to obtain the actual sequence. Therefore, the amino acid sequence is not obvious under *in re Deuel.*

In addition, Applicants reiterate that because it does not disclose the amino acid sequence of the G-protein β subunit described therein, the Bruch *et al.* reference fails to teach one of skill in the art how to make and use this G-protein β subunit. Therefore, the Bruch *et al.* reference is non-enabling for the purpose of determining whether the present invention is obvious in view of the above cited references. This point is further enforced by the fact that there is no established connection between Bruch's G-protein β subunit and the amino acid sequences disclosed in the Ray and Levine references.

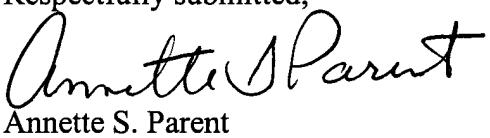
In summary, Applicants contend that the obviousness rejection is improper and respectfully request the withdrawal of this rejection.

CONCLUSION

In view of the foregoing, Applicants believe all claims now pending in this Application are in condition for allowance. The issuance of a formal Notice of Allowance at an early date is respectfully requested.

If the Examiner believes a telephone conference would expedite prosecution of this application, please telephone the undersigned at 415-576-0200.

Respectfully submitted,



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